

# Two New Studies Show Quercetin Improves COVID Outcomes

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## STORY AT-A-GLANCE

- › Two recently published studies confirm quercetin is useful as an adjunct therapy in the early outpatient treatment of mild SARS-CoV-2 infection
- › In one study, COVID patients who received quercetin in addition to analgesics and an antibiotic cleared the virus faster than those who only received analgesics and antibiotics, and a greater number of patients reported reduced symptoms
- › In the second study, daily quercetin supplementation for one month reduced the frequency and length of hospitalization, the need for noninvasive oxygen therapy, intensive care and deaths
- › Quercetin has antiviral, anti-blood clotting, anti-inflammatory and antioxidant properties, all of which are important in the treatment of SARS-CoV-2 infection
- › Quercetin also inhibits binding of specific spike proteins to your ACE2 receptors, thereby blocking the virus' ability to infect your cells. It's also been shown to directly neutralize viral proteins that are critical in the replication of SARS-CoV-2

In an August 21, 2021, newsletter,<sup>1</sup> Dr. Michael Murray discussed the use of quercetin for respiratory infection symptoms. In November 2020, he'd suffered a "very mild and brief bout of COVID-19," and one of his "secret weapons," he believes, might have been quercetin.

He also recounts an anecdotal story of a friend who developed suspicious respiratory symptoms. His friend had been taking a number of supplements said to offer protection, but was still feeling awful.

As it turns out, the one thing he'd not taken was quercetin, and as soon as he did, that same day, his symptoms started to dissipate. This experience, Murray says, "is consistent with the results from two clinical trials" that were recently published.

Quercetin seems to be a safe, far less expensive, and easier-to-obtain alternative to hydroxychloroquine, and it works by a similar mechanism, driving zinc into the cells to stop viral replication.

## **Statistical Improvement in Clinical Outcomes**

In the first study,<sup>2</sup> 42 COVID-19 outpatients were divided into two groups. One group of 21 patients received standard medical therapy consisting of analgesics and an antibiotic (acetaminophen 500-milligram (mg) to 1,000-mg dose if body temperature was higher than 37.5 degrees C – 99.5 F – with a maximum daily dosage of 3 grams, and 500 mg azithromycin for three consecutive days).

The other group of 21 patients received standard therapy plus the equivalent of 600 mg of quercetin per day (divided into three doses) for seven days, followed by another seven-day course of 400 mg of quercetin per day (divided into two doses).

The quercetin used was a brand name formulated with sunflower lecithin, which has been demonstrated to increase absorption in the gut by as much as 20 times, compared to pure quercetin formulations.

The main outcomes being evaluated were virus clearance and symptoms. After one week of treatment, 16 of the 21 patients in the quercetin group tested negative for SARS-CoV-2 and 12 reported that all symptoms had diminished.

In the standard care group, only two tested negative and four had partially improved symptoms. By the end of Week 2, the five remaining patients in the quercetin group

tested negative. In the standard care group, 17 of the 19 remaining patients tested negative and one had died.

As noted by the authors, quercetin supplementation “statistically shortens the timing of molecular test conversion from positive to negative, reducing at the same time symptoms severity and negative predictors of COVID-19.”

“These results are impressive and hopefully additional studies will be conducted on hospitalized patients to see how quercetin might be helpful in more severe cases,” Murray wrote in his newsletter.

## **Quercetin Reduces Hospitalizations and Deaths**

The second study<sup>3</sup> – a prospective, randomized, controlled and open-label trial – gave 152 COVID-19 outpatients a daily dose of 1,000 mg of quercetin for 30 days to evaluate its adjuvant effects in the treatment of early symptoms and the prevention of severe infection. According to the authors:

*“The results revealed a reduction in frequency and length of hospitalization, in need of non-invasive oxygen therapy, in progression to intensive care units and in number of deaths. The results also confirmed the very high safety profile of quercetin and suggested possible anti-fatigue and pro-appetite properties.*

*QP (Quercetin Phytosome®) is a safe agent and in combination with standard care, when used in early stage of viral infection, could aid in improving the early symptoms and help in preventing the severity of COVID-19 disease. It is suggested that a double-blind, placebo-controlled study should be urgently carried out to confirm the results of our study.”*

## **Mechanisms of Action**

As noted in the first study<sup>4</sup> above, quercetin was chosen based on the fact that it has antiviral, anti-blood clotting, anti-inflammatory and antioxidant properties, all of which

are important in the treatment of SARS-CoV-2 infection. In the second study, more detailed mechanisms of action are reviewed. According to the authors:<sup>5</sup>

*“SARS-CoV-2 proteases, like 3-chymotrypsin-like protease (3CLpro), papain-like pro-tease (PLpro), RNA-dependent RNA polymerase, spike (S)protein and human angiotensin-converting enzyme 2 (hACE2) are considered possible targets for developing effective anti-COVID-19 drugs.*

*Recently, molecular docking studies have suggested the possible binding interaction of quercetin with the 3CLpro, PLpro, and S-hACE2 complex. Some recent results, obtained by biophysical techniques, appear to support the results of the molecular docking studies.*

*Quercetin, a flavonol not naturally present in the human body, is the most abundant polyphenol in fruits and vegetable and is widely used as a dietary supplement to boost the immune system and promote a healthy lifestyle.*

*Quercetin is characterized by three crucial properties: antioxidant, anti-inflammatory and immunomodulatory. The combination of these actions allows quercetin to be a potential candidate to support all unhealthy conditions where oxidative stress, inflammation and immunity are involved.”*

Initially, quercetin gained attention as a potential treatment against SARS-CoV-2 infection because it's a zinc ionophore, meaning it shuttles zinc – which has well-known antiviral effects – into your cells just like the drug hydroxychloroquine.

**“ In particular, quercetin exerts significant inhibition on the binding of specific spike proteins to ACE-2 receptors, thereby blocking the ability of the virus to infect human cells. Quercetin has also been shown to directly neutralize viral proteins the are critical in the replication of SARS-CoV-2. ~ Dr. Michael Murray”**

Some proposed the primary reason hydroxychloroquine and quercetin worked was because of this feature. Of course, you also had to take zinc along with either of them. To effectively act as a zinc ionophore, the quercetin also needs vitamin C.

Since then, other studies, including the two reviewed here, have shown quercetin has other actions that makes it useful against SARS-CoV-2 as well. As reported by Murray in his newsletter:

*“In particular, quercetin exerts significant inhibition on the binding of specific spike proteins to ACE-2 receptors, thereby blocking the ability of the virus to infect human cells. Quercetin has also been shown to directly neutralize viral proteins the are critical in the replication of SARS-CoV-2.”*

In some studies, quercetin has also been shown to inhibit the release of inflammatory cytokines, which could help alleviate infection-related symptoms and suppress excessive inflammatory responses from occurring. Its antioxidant effects may also help prevent tissue damage caused by scavenging free radicals, thereby aiding in the recovery process of viral infections.<sup>6</sup>

## **Quercetin’s Antiviral Properties**

Quercetin’s antiviral properties have been attributed to three main mechanisms of action:

1. Inhibiting the virus’ ability to infect cells
2. Inhibiting replication of already infected cells
3. Reducing infected cells’ resistance to treatment with antiviral medication

For example, research<sup>7</sup> funded by the U.S. Defense Advanced Research Projects Agency (DARPA), published in 2008, found it lowers your risk of viral illness such as influenza and boosts mental performance following extreme physical stress, which might otherwise undermine your immune function and render you more susceptible to infections.

Here, cyclists who received a daily dose of 1,000 mg of quercetin in combination with vitamin C (which enhances plasma quercetin levels<sup>8,9</sup>) and niacin (to improve absorption) for five weeks were significantly less likely to contract a viral illness after bicycling three hours a day for three consecutive days, compared to untreated controls. While 45% of the placebo group got sick, only 5% of the treatment group did.

## **Quercetin Works Against Many Common Viruses**

Before the COVID-19 pandemic struck, several studies had highlighted quercetin's ability to prevent and treat the common cold and seasonal influenza.<sup>10,11,12,13,14,15,16,17,18</sup> By attenuating oxidative damage, it also lowers your risk of secondary bacterial infections,<sup>19</sup> which is actually the primary cause of influenza-related deaths.

Importantly, quercetin increases mitochondrial biogenesis in skeletal muscle, which suggests part of its antiviral effects are due to enhanced mitochondrial antiviral signaling.<sup>20</sup> Quercetin also works against other viruses, as demonstrated in the following studies:

- A 1985 study found quercetin inhibits infectivity and replication of herpes simplex virus type 1, polio-virus type 1, parainfluenza virus type 3 and respiratory syncytial virus (RSV).<sup>21</sup>
- A 2016 animal study<sup>22</sup> found quercetin inhibited mouse dengue virus and hepatitis virus.
- Other studies have confirmed quercetin's power to inhibit both hepatitis B<sup>23</sup> and C<sup>24</sup> infection.
- A March 2020 study<sup>25</sup> found quercetin provides "comprehensive protection" against *Streptococcus pneumoniae* infection, both in vitro and in vivo, primarily by neutralizing pneumolysin (PLY),<sup>26</sup> one of the toxins released from pneumococci that encourages *S. pneumoniae* infection to blossom in the first place.

Streptococcus pneumoniae is responsible not only for pneumonia, but can also be involved in some ear and sinus infections, meningitis and certain blood infections.<sup>27</sup> As reported by the authors of this study:<sup>28</sup>

*“The results indicated that quercetin significantly reduced PLY-induced hemolytic activity and cytotoxicity via repressing the formation of oligomers.*

*In addition, treatment with quercetin can reduce PLY-mediated cell injury, improve the survival rate of mice infected with a lethal dose of S. pneumoniae, alleviate the pathological damage of lung tissue and inhibit the release of cytokines (IL-1 $\beta$  and TNF- $\alpha$ ) in bronchoalveolar lavage fluid.*

*Considering the importance of these events in antimicrobial resistant S. pneumoniae pathogenesis, our results indicated that quercetin may be a novel potential drug candidate for the treatment of clinical pneumococcal infections.”*

## **How Quercetin Combats Inflammation and Boosts Immunity**

Aside from its antiviral activity, quercetin is also known for boosting immunity and combating inflammation. As noted in a 2016 study<sup>29</sup> in the journal Nutrients, mechanisms of action include (but is not limited to) the inhibition of:<sup>30</sup>

- Lipopolysaccharide (LPS)-induced tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) production in macrophages. TNF- $\alpha$  is a cytokine involved in systemic inflammation, secreted by activated macrophages, a type of immune cell that digests foreign substances, microbes and other harmful or damaged components
- LPS-induced mRNA levels of TNF- $\alpha$  and interleukin (IL)-1 $\alpha$  in glial cells, which results in “diminished apoptotic neuronal cell death”
- The production of inflammation-producing enzymes
- Calcium influx into the cell, which in turn inhibits pro-inflammatory cytokine release, as well as histamine and serotonin release from intestinal mast cells<sup>31</sup>

According to this paper, quercetin also stabilizes mast cells, has cytoprotective activity in the gastrointestinal tract, and “a direct regulatory effect on basic functional properties of immune cells,” which allows it to inhibit “a huge panoply of molecular targets in the micromolar concentration range, either by down-regulating or suppressing many inflammatory pathways and functions.”<sup>32</sup>

## **Some Brands Offer Greater Bioavailability**

While quercetin does have potent antiviral effects, in order for it to work effectively you need sufficiently high dosages to raise the level of quercetin in your body’s tissues.

The relatively low absorption rate of quercetin is why a sunflower lecithin formulation, sold under the brand name Quercetin Phytosome® was used in the two featured studies discussed at the beginning of this article. That’s not your only option though.

Research<sup>33</sup> published in the July-December 2021 issue of the Journal of Natural Health Products Research, found Quercetin LipoMicel Matrix™ has the same total absorption rate as Quercetin Phytosome — and higher peak blood levels.

*“Since both of these forms of quercetin produce similar blood levels, they should produce the same effects at equal dosages based upon quercetin content,” Murray wrote in his newsletter, adding:*

*“My dosage recommendation as part of a nutritional supplement program to support immune function in the prevention of COVID-19 is Quercetin LipoMicel Matrix™ 250 mg twice daily.*

*And in patients with active COVID-19, my recommendation is ... six capsules of Quercetin LipoMicel Matrix™ twice a day providing a total of 3,000 mg of quercetin in this enhanced form. This high dosage should be taken for at least 10 days and then reduced to a maintenance dosage of 250 mg twice daily ...*

*[This] high dosage may not be necessary. But my dosage calculations are based upon likely tissue concentrations needed to exert the strongest antiviral effects.*

*And given the safety of quercetin, there is no harm at this level.”*

## Early Treatment Protocol Using Quercetin

One doctor who early on in the COVID pandemic brought quercetin into the limelight was Dr. Vladimir Zelenko. As hydroxychloroquine became difficult to obtain, Zelenko switched to recommending quercetin instead, as it’s readily available as an over-the-counter supplement. For a downloadable “cheat sheet” of Zelenko’s protocol for COVID-19, visit [VladimirZelenkoMD.com](https://VladimirZelenkoMD.com).

## Other Health Benefits of Quercetin

There are also other lesser known benefits and uses for quercetin, including the prevention and/or treatment of:<sup>34</sup>

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High blood pressure<sup>35,36</sup>

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Cardiovascular disease<sup>37</sup>

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Obesity<sup>38</sup> and metabolic syndrome<sup>39</sup> (a cluster of conditions including high blood pressure, high blood sugar, high triglyceride levels and fat accumulation around the waist that raise your risk for Type 2 diabetes, heart disease and stroke)

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Certain kinds of cancer, in particular leukemia, and to a lesser degree breast cancer<sup>40</sup>

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Nonalcoholic fatty liver disease (NAFLD)<sup>41</sup>

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Gout<sup>42</sup>

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Arthritis<sup>43</sup>

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Mood disorders<sup>44</sup>

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Aluminum-induced neurodegenerative changes, such as those seen in Alzheimer’s,

Parkinson's and amyotrophic lateral sclerosis (ALS).<sup>45</sup>

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Longevity, thanks to its senolytic benefits (clearing out damaged and worn-out cells)<sup>46,47</sup>

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Research has also highlighted quercetin's epigenetic influence and ability to:<sup>48</sup>

- Interact with cell-signaling pathways
- Modulate gene expression
- Influence the activity of transcription factors
- Modulate microRNAs

MicroRNAs used to be considered "junk" DNA. But far from being useless, research has revealed so-called "junk" DNA is actually microRNA and plays a crucial role in regulating genes that make the proteins that build your body.

The microRNA function as "on/off" switches for the genes. Depending on the microRNA input, a single gene can code for any of more than 200 protein products. Quercetin's ability to module microRNA may also help explain its cytotoxic effects, and why it appears to improve cancer survival (at least in mice).

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